PATENT ABSTRACTS OF JAPAN

(11)Publication number : 08-133943
(43)Date of publication of application : 28.05.1996

(51)Int.Cl. A61K 7/48
A61K 7/00
A61K 38/22
A61K 38/27

(21)Application number : 06-293679
(22)Date of filing : 04.11.1994

(71)Applicant : KYODO NYUGYO KK
(72)Inventor : OISHI HIFUMI
TANI HISANORI
HATTORI TAKASHI

(54) SKIN BEAUTIFIER

(57)Abstract:
PURPOSE: To obtain a skin beautifier containing, as active ingredient(s), a fraction containing respective growth factors from the milk of a monogastric animal such as humans or a ruminant such as cattle, having skin beautifying effects of the respective growth factors on the cells and skin.
CONSTITUTION: This skin beautifier contains, as active ingredient(s), a whey fraction of ruminant initial milk or monogastric animal milk each containing insulin-like growth factor, transformation growth factor and fibroblast growth factor, or a cream fraction, milk fat globule membrane and butter milk fraction of ruminant or monogastric animal milk, each containing fibroblast growth factor and heparan sulfate proteoglycan.

* NOTICES *

CLAIMS

[Claim(s)]
[Claim 1]A lustrous skin agent making into an active principle a whey fraction of ruminant colostrum containing an insulin like growth factor, a transformation growth factor, and a fibroblast growth factor.
[Claim 2]A lustrous skin agent making into an active principle a whey fraction of monogastric animal milk containing an insulin like growth factor, a transformation growth factor, and a fibroblast growth factor.
[Claim 3]A lustrous skin agent making into an active principle rumination or a cream fraction of monogastric animal milk, milk fat globule membrane, and a butter milk fraction containing a fibroblast growth factor and heparan sulphate proteoglycan.

[Translation done.]

* NOTICES *

1.This document has been translated by computer. So the translation may not reflect the original precisely.
2.**** shows the word which can not be translated.
3.In the drawings, any words are not translated.

DETAILED DESCRIPTION

[Detailed Description of the Invention]
[0001]
[Industrial Application]This invention obtains the fraction containing each growth factor from the milk of the single stomachs, such as Homo sapiens and a cow, and a ruminant, and relates to the lustrous skin agent which demonstrates the beautiful skin effect over each cell and skin.
[0002]
[Description of the Prior Art]Various growth factors are contained in the milk of mammalian, and it is indispensable to healthy growth of the newborn infant of a seed respectively. For example, in Homo sapiens and the cow which are most often studied. The growth factor accepted in common with Homo sapiens and cow milk, IGF (an insulin like growth factor, Francis, G.L. et al. Biochem. J., and 251.95-103 (1988).) Rinderknecht, E., Proc. Natl. Acad. Sci. USA, 73, 2365-2369 (1976), TGF (a transformation growth factor, Noda, K. et al., Gann, 75, and 109-112 (1984).) David, Y. J. et al., J.Protein Chemistry, 10, 565-575 (1991), And they are aFGF and bFGF (acidity, and a basic fiber bud growth factor, artificer unpublished), It is reported that EGF (epidermal growth factor) is observed only in Homo sapiens milk, and there is not [exist and] in cow milk (Shing. Y. W. et al., Endocrinology, 115, 273-282 (1984)).
[0003]The cell singularity of these each growth factor is very low, and acts on a wide range cell. Immunosuppression (Tsunawa K, S. et al., Nature, 334, 260-262, (1988)) and connective tissue by TGF-beta inactivating a macrophage in addition to growth, for example in the range, composition of the collagen fibronectin and proteoglycan which are the basic components of an extracellular matrix is promoted (Kovacs, E. J. et al., Immunol, Today12, and 17 (1991).) Kelley, J., and Am. Rev. Respir. Dis.141 and 765 (1990) -- things are checked. These each growth factor forms the network which is not acting separately and acts mutually.
[0004]
[Problem(s) to be Solved by the Invention]Therefore, in order to expect a beautiful skin effect, naturally those [rather than] who use it as a mixture in the form nearer to nature are independently expected that the effect is more expectable using each growth factor.
[0005]If each growth factor of Homo sapiens and a cow is compared, the homology on these primary structures will be dramatically high, will almost be the same, and will act on the cell between different species similarly. From these standpoints, artificers got the fraction containing each growth factor from Homo sapiens and cow milk, influence on each cell and skin was investigated, and the beautiful skin effect found out the dramatically high thing, and completed this invention.
[0006]
[Means for Solving the Problem]That is, in this invention, the lustrous skin agent according to claim 1 makes an active principle a whey fraction of ruminant colostrum containing an insulin like growth factor, a transformation growth factor, and a fibroblast growth factor. The lustrous skin agent according to claim 2 makes an active principle a whey fraction of monogastric animal milk containing an insulin like growth factor, a transformation growth factor, and a fibroblast factor. The lustrous skin agent according to claim 3 makes an active principle rumination or a cream fraction of monogastric animal milk, milk fat globule membrane, and a butter milk fraction

containing a fibroblast growth factor and heparan sulphate proteoglycan.
[0007]
[Function]The whey fraction of the ruminant colostrum containing an insulin like growth factor, a transformation growth factor, and a fibroblast growth factor or monogastric animal milk is made into an active principle, Or a lustrous skin agent is manufactured by making into an active principle the rumination or the cream fraction of monogastric animal milk, the milk fat globule membrane, and the butter milk fraction containing a fibroblast growth factor and heparan sulphate proteoglycan.
[0008]
[Example]Next, an example explains this invention in detail.
example 1. method-of-preparation [of Homo sapiens milk wells]: -- by centrifugal separation, the milk to two weeks of post partum was divided into cream and skim milk. The degreasing lump was removed from cream by the churning method, the butter milk fraction was obtained, and decasein was carried out with pH 4.6 or an ethanol sedimentation method. It freeze-dried, after desalting by the ultrafiltration module of the cut off molecular weight 3,000, or permeable membrane. This was made into Human butter milk derived FGF (HBM-FGF), and the experiment was presented. After skim milk added $CaCl_2$ and ethanol so that the last calcium concentration and ethanol might be set to 0.05-0.1M to 10 to 20%, and it adjusted pH to 6.0, it was warmed at 40 **. The produced sediment was removed by centrifugal separation, digestive liquor was contacted to retinoic acid fixed amino SERURO fine resin (made by RA-SERURO fine ** Seikagaku), and beta-lactoglobulin was removed. It freeze-dried, after desalting the RA-SERURO fine resin non-adsorbate using the ultrafiltration module (made by Asahi Chemical Co., Ltd.) of the cut off molecular weight 3,000. This was made into Humanskim milk derivedgrowth factors (BCSM-GFs), and the experiment was presented.
[0009]example 2. preparation [of cow milk wells]: -- the milk within post-partum 24 hour by the method of a statement in The Example 1, [adjust and] The cream fraction origin is made into bovine colostrum butter milk derived FGF (BCBM-FGF), The thing of skim milk origin was made into bovine colostrum skim milk derived growthfactors (BCSM-GFs), and the experiment was presented.
[0010]example 3. growth factor activity [of each adjustment thing]: -- HBM-FGF and BCBM-FGF measured activity at HSM-GFs and BCSM-GFs counting those cell numbers for the activity over cow umbilical cord endothelial cells using a mouse BALB/C 3T3 cell.
[0011]a) HBM-FGF and BCBM-FGF:cell-growth activity -- the enzymatic process (the volumes for Yoji Mitsui.) from a cow umbilical cord Endothelial cells were obtained by separation and culture (1987) of a functional cell, and 227-229, and 3rd generation preliminary culture was carried out under the conditions of 37 ** and 5%CO_2 by FCS ** RPMI 1640 culture medium (made by Gibco) 10%. After having planted so that it might become a cell number of 50 piece / hole at 96 hole microplate (made by a falcon company), and replacing by a serum free medium (RPMI 1640), HBM-FGF and BCBM-FGF were added so that it might become 0-3% concentration, and it cultivated for 48 hours - 72 hours, and the cell number of each hole was counted. The result was shown in drawing 1.
[0012]HSM-GFs and BCSM-GFs : b) Cell-growth activity in a MEM culture medium (made by Gibco). The 3T3 cell which carried out preliminary culture under the above-mentioned conditions was planted in 96 hole microplate on the conditions described in (a), HSM-FGs and BLSM-GFs were added so that it might become 0-3% concentration, and it cultivated under the same conditions, and the cell number of each hole was counted. The result was shown in drawing 2.
[0013]Extracellular-matrix composition ability measured the content of collagen, hyaluronic acid (HA), and heparan sulphate proteoglycan (HSPG). That is, it plants in a dish (made by a falcon company) with a 3T3 cell diameter of 80 mm, HSM-GFs and BLSM-GFs were added to non-blood serum RPMI 1640 culture medium so that it might become 0-3% concentration, respectively, the cell cultured until the cell number became confluent under the conditions of a statement at (a) was exfoliated using EDTA, and the extracellular matrix adhering to a dish was obtained. Collagen is an electrophoresis method and HA and HSPG were measured with

nitrocellulose membrane two dimensional electrophoresis. A result is shown in Table 1.
[0014]
[Table 1]

	BSM-GFs添加(%)				BCSM-GFs添加(%)			
	0	1	2	3	0	1	2	3
コラーゲン	−	±	++	+++	−	+	++	+++
HA	−	±	+	++	−	+	+	++
HSPG	−	−	+	+	−	+	+	+

−：陰性 ±：疑陽性 +,++,+++：陽性(活性の強さをあらわす)

[0015]example 4. surface deterioration improvement effect: -- xylene was applied to 23 ** and 5 mm of regions-of-back ^{2} of the mouse on the 4th, and the mouse of 16 weeks old after the birth bred at humidity 50%, and it was made ruined The gauze into which 500 ml of BCSM-GFs 1% ******** solutions were infiltrated was applied 16 hours afterward, and it bred under the same 48-hour conditions. As contrast, xylene was applied to 5 mm of regions-of-back ^{2} of the same solid, an equivalent amount of commercial essences were applied under the same conditions, and it bred under the same conditions for 48 hours. A judgment observes the state of the skin macroscopically and is ********. A result is shown in Table 2.
[0016]
[Table 2]

	肌荒れ改善効果
対照（美容液のみ）	−
BLSM-GFs 1%添加美容液	+

−：効果なし +：効果あり

[0017]example 5. allergy improvement effect and antiallergic action: -- metal was contacted to the left arm of the volunteer of the metallic contact sex skin skin allergosis, and inflammation was made to induce The same BCSM-GFs addition as what was used for Example 4 after that, and an additive-free essence were applied, and the improvement effect was observed macroscopically. The essence same just before inducing inflammation was applied, and the inflammatory reaction at the time of contacting metal was observed macroscopically. A result is shown in Table 3.
[0018]
[Table 3]

	治療効果	予防効果
対照（美容液のみ）	−	−
BCSM-GFs 1%添加美容液	+	+

−：効果なし +：効果あり

[0019]
[Effect of the Invention]The antiallergic action was obtained with the improvement effect of surface deterioration by the lustrous skin agent by this invention.

[Translation done.]